

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Page 5

PATENT

Attorney Docket No.: HIRA1140

REMARKS

Claims 1 to 14 are pending and under examination. In the present communication, claims 1, 2, 3, 5 and 10 have been amended, claims 9 and 14 have been canceled and new claims 15 to 20 have been added. Exhibit A, submitted herein, presents the claims with markings to show changes made.

The amendments submitted herewith are supported by the specification and original claims and do not add new matter. The amendments do not require a new search or raise new issues for consideration because they merely address issues already raised by the Examiner or define Applicants' invention more clearly. It is submitted that the amendments place the claims in condition for allowance or in better condition for appeal by reducing the number of issues for consideration on appeal. The amendments were not made earlier in the prosecution because it is maintained that the previously pending claims were allowable. Since the amendments and new claim do not add new matter or require a new search or consideration, and place the claims in condition for allowance or in better condition for appeal, entry of the amendments is respectfully requested.

Specifically, new claims 15 to 20 do not contain new matter, but further clarify the invention. These new claims are fully supported by the specification, as originally filed. Support for claim 15 may be found, for example, at page 19, lines 23 to 27. Support for claim 16 may be found, for example, at page 20, lines 3 to 4. Support for claim 17 may be found, for example, at page 22, lines 2 to 5 and page 23, lines 2 to 16. Support for claim 18 may be found, for example, at page 23, lines 10 to 17. Support for claim 19 may be found, for example, at page 23, lines 2 to 16.

In response to the queries regarding claims 9 and 14, it is noted that claims 9 and 14 have been cancelled herein, and therefore, the queries will not be addressed further.

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Page 6

PATENT

Attorney Docket No.: HIRA1140

Rejections Under 35 U.S.C. § 112, second paragraph

The rejection of claims 1 to 14 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite is respectfully traversed.

Claim 1 is asserted as confusing because the period of heating is uncertain, and the timing of the addition of fumaric acid is unclear. Applicants respectfully submit that those of skill in the art would understand the method steps contemplated by the claim language. However, in order to facilitate prosecution and reduce the issues on appeal, claim 1 (and claims dependent therefrom) have been amended to clearly describe the heating step and the temperature at the time of the addition step.

Specifically, claim 1 has been amended to clarify that the heating is carried out until the temperature of the solution is between 50 and 130°C. This amendment is fully supported in the specification at, for example, page 13, line 26 to page 14, line 10. Claim 1 has also been amended to clarify that in the present invention, fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension are added to the solution and a shearing force is applied to the solution, while maintaining the temperature of the solution between 50°C and 130°C. This amendment is fully supported in the specification, as filed, for example at page 14, lines 9-10 and 22 to 24, page 16, lines 1 to 4.

Claim 10 is asserted to be vague and indefinite because it is unclear from what temperature the solution in claim 10 is cooled. Applicants respectfully submit that those of skill in the art would understand what the steps contemplated by the language of claim 10. However, in order to facilitate prosecution and reduce the issues on appeal, claim 10 (and claims dependent therefrom) have been amended to clearly describe the heating and cooling process in claim 10.

Specifically, claim 10 has been amended to clarify that the solution in claim 10 has first been heated to a temperature of 50°C to 130°C prior to the cooling step. It is respectfully asserted that claim 10 is clear.

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Page 7

PATENT

Attorney Docket No.: HIRA1140

In regard to claim 3, Applicants have amended the claim as suggested by the Examiner to recite "maintained."

In view of the amendments and remarks above, Applicants respectfully request reconsideration and withdrawal of the rejections of claim 1 to 14 under 35 U.S.C. § 112, second paragraph.

Rejection Under 35 U.S.C. §103

The rejection of claims 1 to 14 under 35 U.S.C. § 103 as allegedly obvious over Nore, *et al.* (United States Patent No. 5,530,160, hereinafter "Nore"), in combination with the Brun, *et al.*, (United States Patent No. 5,488,155), Pavia, *et al.* (Introduction to Organic Laboratory Techniques, W.B. Saunders Company, hereinafter "Pavia"), and Tan, *et al.* (United States Patent No. 4,900.821, hereinafter "Tan") is respectfully traversed.

Nore, *et al.* discloses a process of preparing aspartic acid wherein alcoholic fumaric acid is added to ammonium aspartate followed by heating to about 50° C and crystallization of a homogenous solution at a temperature of about 25° to 100° C. However, Nore, *et al.* demonstrate that the use of fumaric acid in an alcoholic solution makes it possible to increase the L-aspartic acid yield. Additionally, Nore, *et al.* does not require a crystallization operation on the L-aspartic acid before filtration (col. 1, lines 18-22), rather the L-aspartic acid formed precipitates and crystallizes instantaneously (col. 1, lines 49-50) upon filtration. Therefore, Nore, *et al.* teaches that the precipitates and crystals of L-aspartic acid are obtained without steps of heating and crystallizing.

Additionally, while Nore, *et al.* indicates a cooling range from 50°C to 30°C, there is no indication of the time in which that cooling occurs. Nore, *et al.* disclose that after stirring for 15

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Page 8

PATENT

Attorney Docket No.: HIRA1140

minutes, the mixture is cooled to 30°C. Therefore, the 15 minute period is a period for stirring, not cooling. The time over which such cooling would occur to optimize the crystallization of the desired product is not well known to one of skill in the art.

As set forth above, the present invention can be distinguished from the Nore, *et al.* reference due to the failure of Nore, *et al.* to teach crystallization prior to filtration, and the failure to disclose a time frame for the cooling to optimize crystallization of the desired product.

It is alleged that Nore, *et al.*, in view of Brun, *et al.* is obvious. This rejection is respectfully traversed. As set forth by the Examiner, Brun, *et al.* teaches a similar process for preparing L-aspartic acid, using a temperature of 135°C and gradual cooling of the reaction products. However, as in Nore, *et al.*, there is no teaching or suggestion regarding the time frame for the gradual cooling. Further, Brun, *et al.* disclose that the temperature of the reaction mixtures were maintained at 20°C, 100°C, and 135°C, with the mixture at 20°C yielding the best results (Table I). Accordingly, even in combination, the Nore, *et al.* and Brun, *et al.* references do not teach the gradual cooling of the present invention.

Similarly, Pavia, *et al.* or Tan, *et al.*, in combination with Nore, *et al.* do not teach or suggest all of the claimed elements of the present invention. These references discuss the removal of a solvent in a crystallization process and the use of recycling to maximize yield of a crystallized product, but neither in combination, with Nore, *et al.* teaches the gradual cooling of the present invention.

As set forth above, none of the cited references, alone or in combination teach or suggest a method for producing L-aspartic acid, comprising: treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution, heating the solution to 50-130°C, adding fumaric acid to the ammonium L-aspartate solution, applying a shearing force to the

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Page 9

PATENT

Attorney Docket No.: HIRA1140

resultant mixture to obtain homogenous solution, and crystallizing L-aspartic acid from the homogenous solution by cooling the solution at an optimum rate. Accordingly, it is respectfully requested that the rejection be withdrawn.

No fee is deemed necessary in connection with the filing of this response. However, if any fee is deemed necessary, the Commissioner is authorized to charge (or apply any credits to) Deposit Account No.: 50-1355. The Examiner is invited to contact Applicants' undersigned representative if there are any questions related to this matter.

Respectfully submitted,

Date:

9/19/01



Lisa A. Haile, J.D., Ph.D.

Registration No. 38,347

Telephone: (858) 677-1456

Facsimile: (858) 677-1465

GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1600
San Diego, California 92121-2189

USPTO Customer Number 28213

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

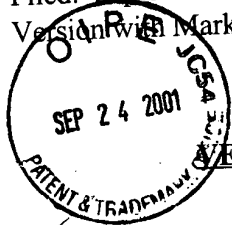
Version with Markings - Page 1

PATENT
Attorney Docket No.: HIRA1140

RECEIVED

SEP 26 2001

TECH CENTER 1600/2900



VERSION WITH MARKINGS TO SHOW CHANGES MADE

3. (Amended) A method for producing L-aspartic acid comprising:
treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution;
[heating to 50 to 130°C said ammonium L-aspartate solution] heating said ammonium L-aspartate solution until a temperature of said solution reaches a range of between 50 to 130°C;
adding [fumaric acid] fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension to said heated ammonium L-aspartate solution in a molar ratio of 0.4 to 0.8 to the total amount of fumarate and the L-aspartate contained therein to form a resultant mixture[;] and applying a shearing force to the resultant mixture to obtain a homogenous solution, while maintaining the temperature of said solution between 50°C and 130°C; [and
crystallizing L-aspartic acid from said homogenous solution to obtain a suspension containing L-aspartic acid crystals] cooling or permitting cooling of said homogenous solution to crystallize L-aspartic acid, thereby obtaining suspension containing L-aspartic acid; and
separating L-aspartic acid crystals from said suspension.
4. (Amended) The method according to claim 1, wherein the temperature of said suspension containing L-aspartic acid crystals is in the range from 25 to 100°C when the [deposited] crystallized L-aspartic acid is separated therefrom.
3. The method according to claim 1, wherein said homogenous solution is [retained] maintained at 50 to 130°C for 0.1 second to 1 hour.

Applicants:

Mukouyama et al.

Application No.: 09/408,142

Filed: September 29, 1999

Version with Markings - Page 2

PATENT

Attorney Docket No.: HIRA1140

5. (Amended) The method according to claim 1, wherein [said resultant mixture is cooled] said cooling step is performed at a rate of 0.1 - 5°C /min from the temperature at which [fumaric acid] fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension is added thereto to the temperature at which crystallized L-aspartic acid is separated therefrom, to thereby [deposit] crystallize L-aspartic acid.
11. (Amended) A method for producing L-aspartic acid comprising:
treating an ammonium fumarate solution with aspartase to generate an ammonium L-aspartate solution;
heating said ammonium L-aspartate solution until a temperature of said solution reaches a range of between 50 to 130°C;
adding [fumaric acid] fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension to said ammonium L-aspartate solution; and
[cooling the resultant mixture at a rate of 0.1-5°C/min to crystallize L-aspartic acid]
cooling or permitting cooling of said resultant mixture at a rate of 0.1 to 5 °C/min from the temperature at which fumaric acid dry crystals, moisture-containing fumaric acid crystals, or fumaric acid aqueous suspension is added thereto to crystallize L-aspartic acid for crystallizing L-aspartic acid, thereby obtaining suspension containing L-aspartic acid; and
separating L-aspartic acid crystals from said suspension..